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Phenotypic expressions of CCR5-delta32/delta32 homozygosity.

Nguyen GT, Carrington M, Beeler JA, Dean M, Aledort LM, Blatt PM, Cohen AR, DiMichele D, Eyster ME, Kessler CM, Konkle B, Leissinger C, Luban N, O'Brien SJ, Goedert JJ, O'Brien TR.

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OBJECTIVE: As blockade of CC-chemokine receptor 5 (CCR5) has been proposed as therapy for HIV-1, we examined whether the CCR5-delta32/delta32 homozygous genotype has phenotypic expressions other than those related to HIV-1. **DESIGN:** Study subjects were white homosexual men or men with hemophilia who were not infected with HIV-1. In this study, 15 CCR5-delta32/delta32 homozygotes were compared with 201 CCR5 wild-type (+/+) subjects for a wide range of clinical conditions and laboratory assay results ascertained during prospective cohort studies and routine clinical care. CCR5-delta32 genotype was determined by polymerase chain reaction, followed by single-stranded conformational polymorphism analysis. **RESULTS:** Hypertension and conditions attributable to hemophilia were the only diagnoses frequently found in clinical records of CCR5-delta32/delta32 study subjects. Based on blood pressure measurement and treatment history, CCR5-delta32/delta32 homozygotes had a 2.8-fold higher prevalence of hypertension than age-matched CCR5-+/+ study subjects (95% confidence interval [CI], 1.2-6.4; $p = .01$); none of the homozygotes had severe hypertension. Hematologic measures were generally similar across the genotypes, but total lymphocyte counts were approximately 20% higher in CCR5-delta32/delta32 study

subjects than in CCR5-+/+ study subjects ($p < .05$). Among patients with hemophilia who were infected with hepatitis C virus (HCV), mean alanine aminotransferase levels were 117% higher among CCR5-delta32/delta32 homozygotes ($p < .05$), but serum HCV levels did not differ by CCR5-delta32 genotype. CCR5-delta32/delta32 homozygous study subjects had a lower prevalence of antibodies to measles virus than those with other genotypes, but this association was not confirmed in a group of blood donors. The prevalence of antibodies to nine other common viruses, HBV, and HCV was not related to CCR5 genotype. CONCLUSIONS: CCR5-delta32/delta32 homozygotes are generally similar to wild-type persons. Confirmatory investigations are required to determine whether hypertension, increased lymphocyte counts, and higher hepatic enzyme levels in the presence of HCV infection represent true phenotypic expressions of this genotype. CCR5-delta32/delta32 homozygosity does not provide broad protection against viral infections.

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